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Cognitive function, quality of life, and aging: relationships in individuals with and without spinal cord injury

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Abstract

Background: Correlations between aging, cognitive impairment and poor quality of life (QOL) have been observed for many patient populations.

Objective: The purpose of this study was to examine these correlations in individuals with and without spinal cord injury (SCI).

Methods: 23 individuals with complete SCI and 20 individuals without SCI ("NON") underwent assessment of cognitive function via the NIH Toolbox for Neurological and Behavioral Function. Participants self-rated QOL via global and symptom/domain-specific measures.

Results: SCI rated global QOL to be lower than NON for the EQ-5D QALY ($p < .001$), but not the EQ-5D VAS, which imposes no penalty for wheeled mobility. Low QOL clustered mainly in domains pertaining to physical function/symptoms. Participants with SCI reported high QOL for positive affect/well-being and resilience. Cognitive function in SCI did not differ from NON. However, strong correlations between age and cognition observed in NON (all $R^2 > 0.532$) were absent in SCI. Significant correlations between cognition and QOL were prevalent for NON but not for SCI.

Conclusions: Dissociation of age, cognition and QOL occurred with SCI. Divergence between EQ-5D QALY and VAS suggests that individuals with SCI may recalibrate personal assessments of QOL in ways that minimize the importance of mobility impairment.

Keywords

Cognition; executive function; memory; resilience; participation

Introduction

Despite decades of advancements in medical management and rehabilitation, people living with spinal cord injury (SCI) often report poorer quality of life (QOL) than the general population (Migliorini, New, and Tonge, 2011). Much effort has been directed at uncovering

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Declaration of Interest

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the factors that undermine health and well-being for these individuals. Secondary health conditions of SCI exert a strong negative effect on QOL (Lidal, Veenstra, Hjeltnes, and Biering-Sorensen, 2008), potentially eclipsing factors such as the absolute level of physical functional impairment (Krahn, Suzuki, and Horner-Johnson, 2009) or the influence of aging (Barker et al., 2008; Lidal, Veenstra, Hjeltnes, and Biering-Sorensen, 2008). Psychosocial factors such as depression and anxiety correlate negatively with QOL, while other traits such as resilience and self-efficacy exert a positive effect (Guest et al., 2015). Adding complexity to this interplay of physical and emotional factors, personal definitions of QOL and life priorities may shift after SCI (Simpson, Eng, Hsieh, and Wolfe, 2012). Individuals may substantially recalibrate their expectations and personal assessments in the first years post-injury (Schwartz et al., 2018). In this changing milieu, numerous knowledge gaps exist for how medical, psychological, and rehabilitation interventions can offer the best assistance. Therapeutic targets for enhancing QOL after SCI are needed by all elements of the post-SCI care team.

In several patient populations, cognitive impairment has been identified as a potential point of intervention for protecting and improving QOL. Links between cognitive impairment and negative QOL have been reported for: hospitalized elderly individuals (Saracli et al., 2015); patients with stroke (Cumming, Brodtmann, Darby, and Bernhardt, 2014); mild/subjective cognitive decline (Hill et al., 2017); cardiac arrest (Orbo et al., 2015); and multiple sclerosis (Grasso et al., 2017). Cognitive impairment appears to be common after SCI, occurring in ~29% of individuals with SCI in a recent study (Craig, Guest, Tran, and Middleton, 2017). Impairments in cognitive processes such as motor sequence learning (Bloch, Tamir, Vakil, and Zeilig, 2016) may be especially problematic if they interfere with post-SCI rehabilitation activities, which are severely time-restricted in many medical systems (Qu, Shewchuk, Chen, and Deutsch, 2011; Shields, 2017).

Whether cognitive impairment is a correlating factor for QOL in patients with SCI has not been previously determined. Recent studies have shown robust links between cognitive capacity and psychological disorders in SCI, suggesting that people with low cognitive function may be at an elevated risk for mood disorders or substance abuse (Craig, Guest, Tran, and Middleton, 2017). It seems plausible that such individuals may also rate their QOL to be lower than individuals who have higher cognitive function. The potential mediating effect of aging on cognitive function after SCI is also uncertain, with some recent evidence emerging for exacerbation of cognitive decline with chronic SCI (Molina et al., 2018). The purpose of this preliminary investigation was to determine whether relationships exist between cognition, QOL, and age in individuals with SCI. To explore whether such relationships may be typical of the general population, or whether they may instead reflect adaptations to life with SCI, the study also examined correlations between QOL and cognition in a non-SCI cohort. We hypothesized that individuals with SCI would experience lower QOL in domains previously shown to be at risk after SCI: depression, anxiety, and resilience (Craig, Guest, Tran, and Middleton, 2017; Guest et al., 2015). As is typical for the non-SCI population (Casaletto et al., 2015), we expected that aging would be negatively associated with cognitive function in participants with SCI. We also hypothesized that, as has been observed in other patient populations, correlations would exist between cognition and QOL in individuals with SCI. If such links exist, cognitive function may

constitute a viable therapeutic target for protecting at-risk QOL domains in people living with SCI.

Methods

Participants

Twenty-three individuals with motor/sensory complete SCI (AIS-A) (Kirshblum et al., 2011) and 20 individuals without SCI participated in the study (Table 1). All participants were recruited from the healthy general population of the local community via brochures, e-mail advertisements, and referral from clinical colleagues. SCI duration ranged from 8 months to 30 years (mean = 11.8 years). This time frame excludes the expected phase of immediate post-SCI rapid QOL change (Mortenson, Noreau, and Miller, 2010). All participants signed an informed consent document approved by the University of Iowa Human Subjects Institutional Review Board. The trial was registered at Clinical Trials Registration: NCT02622295.

Participants with any previous diagnosis of cognitive decline (e.g. dementia), traumatic brain injury, or a neurodegenerative condition (e.g. multiple sclerosis) were excluded. Participants with and without SCI did not differ according to age ($p = .44$). Other potential confounding factors such as sleep apnea, psychotropic medications, and social/environmental context were not examined (Sachdeva, Gao, Chan, and Krassioukov, 2018).

QOL metrics

Participants completed four QOL metrics (Table 2) via REDCap, a secure online survey administration platform (Obeid et al., 2013), using a laboratory computer in a private location. They were free to skip any question and to use their best judgment to answer ambiguous questions. The EQ-5D-5L (Herdman et al., 2011) consisted of 5 questions that yield a quality adjusted life-year (QALY) score representing subjective preference for health states between 0 (dead) to 1 (perfect health) (Szende, Oppe, and Devlin, 2007). Participants also rated their general health on a 100-point visual analog scale (VAS). Unlike the QALY score, the EQ-5D VAS score imposed no “ambulation penalty” by defining mobility specifically as “walking”. The Patient-Reported Outcome Measurement Information System (PROMIS) Global Health scale (Amtmann, Cook, Johnson, and Cella, 2011) included a 10-item short form that incorporated Global Physical and Mental Health sub-scales. The SCI-QOL metric included six fixed-length short-forms (each 8–13 questions) (Tulsky et al., 2015) that were germane to a study of relationships between QOL and cognition: 1) Pain Interference; 2) Positive Affect and Well-Being; 3) Anxiety; 4) Depression; 5) Resilience; and 6) Ability to Participate in Social Roles and Activities. The Spinal Cord Injury Secondary Conditions Scale - Modified (SCS-M) evaluated the presence and severity of 22 common secondary health conditions (SHC’s) of SCI (Lidal, Veenstra, Hjeltnes, and Biering-Sorensen, 2008; Westgren and Levi, 1998) on a scale from 0 (not experienced) to 3 (significant or chronic problem) (Craven, Hitzig, and Mittmann, 2012). The number of SHC’s present and the summed severity ratings of all SHCs were tabulated (Sum Score). Formal statistical comparison of post-SCI QOL to general population normative values was

not undertaken for this study. Instead, general population normative values will be presented to help the reader contextualize the scores of the study cohorts.

Cognitive testing

The National Institutes of Health Toolbox for Neurological and Behavioral Function - Cognition Battery (NIH Toolbox) (Dikmen et al., 2014; Tulsky et al., 2014; Weintraub et al., 2013; Zelazo et al., 2014) is a computerized testing platform for measurement of cognitive function (Table 2). The Dimensional Change Card Sort (DCCS) test provides an estimate of set shifting by having participants match a series of bivalent test pictures according to changing salient dimensions (Zelazo et al., 2014). In the Flanker Inhibitory Control and Attention test, participants identify the left-right orientation of a central arrow among other arrows pointing in the same (congruent) or different (incongruent) direction (Zelazo et al., 2014). For these tests, the participant's score reflects both test accuracy and speed.

The List Sorting Working Memory test evaluates the storage and manipulation of information by requiring subjects to sort and repeat a presented list of items (Baddeley, 1992). The Picture Sequence Memory test evaluates episodic memory by requiring the participant to recall sequences of 6–18 illustrated items (Tulving, 2002). For both of these tests, scores reflect test accuracy with no speed component.

Participants completed NIH Toolbox tests via an iPad app (software version 1.17.1650) that required them to reach forward from a standardized start position to press a keyboard button. Respondents with trunk or arm motor impairment may respond more slowly and therefore achieve a lower score for timed tests (i.e. DCCS and Flanker) or fail to complete timed tests altogether (Cohen et al., 2017). The NIH Toolbox "Reasonable Accommodation Guidelines" offers no alternate test procedure (National Institutes of Health, 2012). To reduce the confounding influence of task motor demands, all participants, including those without SCI, completed the Flanker and DCCS tests with the assistance of a proctor (Lee, Dudley-Javoroski, and Shields, 2019). The addition of the proctor's reaction time increased the time-based vector of participants' scores, negatively biasing the scores. While this mitigated the confounding motor demand, it also prevents statistical comparison of DCCS and Flanker scores with standardized national averages. All cognitive scores were tabulated by the iPad software as Unadjusted and demographically-adjusted ("Fully-Adjusted") scale scores.

Statistical analysis

QOL differences between participants with SCI ("SCI") and without SCI ("NON") were examined via Student's t-tests with Bonferroni adjustment for multiple comparisons (12 QOL scales: $p = .00416$). Differences in cognition were examined in the same fashion (4 Toolbox metrics × 2 scale scores each: Bonferroni-adjusted $p = .00625$). Because of the potential influence of SCI severity on QOL and cognition, a separate set of t-tests to compare participants with quadriplegia (n = 11) to those with paraplegia (n = 12) was conducted (Bonferroni-adjusted $p = .00416$ for QOL, 0.00625 for cognition).

The large number of studied outcome variables, relative to the study sample size, prevented us from using a multivariate regression approach to examine relationships between age, age

at injury, QOL and cognition variables. Pearson's r for each set of variables were instead calculated, with significant associations meeting $p < .05$. SCI duration was not included as a regression variable due to its extensive co-variation with chronological age.

Substantial overlap exists between QOL domains (e.g. mental health and subjective well-being) and most QOL survey metrics cover more than one domain. To examine collinearity among QOL metrics, a correlation matrix was created for all variables, calculating Pearson's r for each pair. Significant correlations met $p < .05$.

Results

By-group comparisons

SCI participants scored significantly lower than NON for the EQ-5D QALY ($p < .001$) but not the VAS ($p = .307$) (Table 3). SCI group QALY scores were > 3 standard error (SE) lower than U.S. normative values, while their VAS ratings were within 1 SE. The SCI group rated their global physical health (PROMIS Physical subscale) lower than NON ($p < .001$) but no differences existed for global mental health (PROMIS Mental subscale). SCI physical health ratings were > 1 SD lower than the U.S. norm (50, SD = 10) but mental health ratings were within 1 SD.

The SCI group reported significantly more SHCs and significantly higher SHC severity than NON (both $p < .001$) (Table 3). On average, participants with SCI reported 8.48 SHCs, with many incidence rates > 50%: involuntary spasms (93.3%); musculoskeletal pain (80.0%); chronic pain (63.3%); sexual dysfunction (63.3%); bladder dysfunction (60.0%); joint contractures (60%); circulatory problems (56.7%); urinary tract infections (56.7%); and bowel dysfunction (53.3%). For the NON group, the only SHC exceeding 25% incidence was musculoskeletal pain (42.9%).

In the SCI-QOL assessment, the SCI group rated their QOL to be poorer than NON for the sub-domains Pain Interference and Ability to Participate in Social Roles & Activities ($p = .0032$, $p = < 0.001$) (Table 3). Interestingly, participants with SCI reported high QOL for Positive Affect and Well-Being (PAWB) and Resilience. Mean PAWB score approached 1 SD above the U.S. mean (50, SD = 10). Participants with SCI rated their Resilience to be nearly 10 scale score points higher than NON, though statistical significance did not emerge because of the strict Bonferroni adjustment applied to this test.

For participants with quadriplegia (QUAD) versus paraplegia (PARA), significant differences existed for EQ-5D QALY ($p < .001$), but not VAS (Table 3). Significant differences between QUAD and PARA also existed for PROMIS physical health ($p = .0041$). Ratings for QUAD were > 1.4 SD below the U.S. population norm, while ratings for PARA were within 1 SD.

Cognitive scores for SCI and NON differed significantly only for the Picture Sequence Fully-Adjusted scale ($p = .0027$) (Table 4). Participants with SCI scored within 0.1 SD of the U.S. normative value (mean = 50, SD = 10), while NON exceeded the U.S. norm by > 1 SD.

No significant differences in cognitive scores existed between the SCI QUAD and PARA subgroups (Table 4).

Correlations between cognition and QOL

Table 5 depicts Pearson correlation coefficients for cognition versus Age and QOL. For NON, all Unadjusted cognitive scores correlated significantly with Age (all $p < .001$). R-squared values ranged between 0.532 and 0.939. Significant correlations between cognition and QOL occurred most frequently for the scales of global QOL (EQ-5D and PROMIS), and for the SCS-M. The EQ-5D VAS correlated significantly with 6 of 8 cognitive scales, with R^2 ranging from 0.234–0.378. PROMIS physical health correlated significantly with 7 of 8 cognitive scales (R^2 from 0.208–0.584). In contrast, PROMIS mental health correlated with no cognitive measures. Significant correlations between the SCS-M and cognitive metrics were widespread, appearing for all cognitive scales except List Sorting-Fully Adjusted. Among SCI-QOL metrics, only the Depression subscale correlated consistently with cognition (6 of 8 scales, R^2 from 0.200–0.349).

In contrast, significant correlations between QOL and cognition were infrequent for participants with SCI. Likewise, the strong association between cognitive metrics and age seen in the NON cohort was absent in the SCI group. For the EQ-5D VAS, the strength of the associations were weaker in the SCI group than in the NON group (all SCI $R^2 < 0.206$; all below the lowest range of NON R^2 values). Major groups of correlations observed in NON (i.e. cognition versus PROMIS physical subscale, SCS-M, and SCI-QOL Depression) were absent in SCI.

In summary, for participants with SCI, an uncoupling appeared to occur between cognition and age, and between cognition and QOL. Table 5 also shows that a partial uncoupling occurred between age and QOL in the SCI group (i.e. age correlated significantly with 5 of 12 QOL metrics for NON, compared to 3 of 12 for SCI). The only correlation observed in both cohorts was between EQ-5D VAS and age; the strength of this correlation was stronger for NON ($R^2 = 0.319$) than for SCI ($R^2 = 0.177$).

Table 6 contains estimates of co-variation (Pearson R^2) for all QOL variables. In general, for participants with SCI, the six SCI-QOL scales correlated significantly among themselves, with the SCS-M measures of secondary health conditions, and with all general QOL measures except the EQ-5D VAS. In particular, the SCI-QOL Anxiety, Depression, and Resilience scales all correlated significantly with all other QOL measures except EQ-5D VAS. The only other measure to show this prevalence of co-variation was the PROMIS Mental Health subscale, which correlated significantly with all metrics except Pain Interference.

In contrast, the prevalence of co-variation among QOL metrics was much lower for the NON participants. In particular, the PROMIS Mental Health sub-scale correlated with no other measure of QOL. The strong correlations observed for SCI-QOL metrics in the SCI cohort were absent, with the partial exception of the Depression scale, which correlated significantly with 6 other metrics.

Discussion

Participants with SCI reported U.S. population-normal levels of Anxiety and Depression and they demonstrated a strong trend toward enhanced Resilience. Low self-reported QOL clustered mainly in domains pertaining to physical function and medical symptoms, as has been consistently observed in other studies (Adriaansen et al., 2016; Noonan, Kopec, Zhang, and Dvorak, 2008; Salem et al., 2014). Correlations between QOL and cognition, which were widespread in non-SCI subjects, were not prevalent in individuals with SCI. A similar dissociation of QOL and cognition has been reported for patients with multiple sclerosis (Baumstarck-Barrau et al., 2011), suggesting that for patients with neurologic impairment, the usual relationships between QOL and cognition may dissociate as other factors gain prominence. This may illustrate the phenomenon of response shift, in which people who face a health state change recalibrate internal standards, reprioritize values, and re-conceptualize the meaning of QOL (Schwartz et al., 2018). Schwartz et al. (2018) recently verified the presence of QOL response shift effects over the first 5 years of SCI in participants who displayed stable cognitive function. These individuals appeared to change their expectations and appraisals of QOL during this time, eventually minimizing links between SCI symptoms and physical and mental functioning. A similar pattern was evident in the present study whereas strong correlations existed between cognition and symptoms (SCS-M) in the NON group, participants with SCI demonstrated no such correlations, despite reporting high rates of symptoms. Response shift effects that diminished the conceptual “weighting” of SCI symptoms may have triggered the dissolution of relationships between cognitive function and this domain of QOL.

Response shift effects may underlie another key difference observed between participants with and without SCI in the present study. Participants with SCI scored significantly lower than NON on the EQ-5D QALY scale. As noted by others (Whitehurst et al., 2016), the wording of the EQ-5D mobility response item imposes a penalty on respondents who do not walk, regardless of their level of adapted mobility. The wording of the EQ-5D VAS imposes no such penalty. Using EQ-5D VAS, participants with SCI rated their global QOL to be no different from participants without SCI or the U.S. normative value. In other words, participants with SCI did not appear to incorporate mobility impairment into their self-assessment of global QOL. This type of mobility recalibration has been noted for a number of preference-based QOL metrics (Dudley-Javoroski and Shields, 2006; Krahn, Suzuki, and Horner-Johnson, 2009). It appears, as stated by Schwartz et al. (2018) that “although individuals with SCI may perceive declines in their physical abilities, they may not perceive these declines as limiting to their daily functioning”.

No previous study has determined whether the usual correlations between age and cognition persist after SCI, or whether they may be eclipsed by other factors. In the present cohort of participants with SCI, no cognitive measure correlated significantly with age; this is in contrast to the strong correlations between age and every cognitive measure in the NON group. In populations without neurologic disease, executive function, working memory, and episodic memory peak between age 20 and 29 and then decline over the remainder of the lifespan (Casaletto et al., 2015). While this relationship might be presumed to persist after SCI, it is important to remember that a number of individual injury-related factors

may strongly influence cognitive performance after SCI. Undiagnosed traumatic brain injury, autonomic dysfunction, and systemic neuro-inflammation are all potential sources of significant inter-individual variation in this population. We believe it is possible that these individual injury-related factors may exert a sufficiently powerful effect on cognition to eclipse the effect of age as a predictor of cognitive function after SCI. As such, rehabilitation specialists should be particularly alert for cognitive impairment caused by injury-specific factors.

A second consideration for rehabilitation specialists is that because individuals with SCI experience QOL response shift, gradually minimizing the importance of mobility impairments, QOL instruments developed for the general population may poorly capture the experience of people living with SCI. This problem is prevalent among QOL instruments, including some that are in widespread clinical use (Krahn, Suzuki, and Horner-Johnson, 2009). When designing survey batteries to measure QOL after SCI, rehabilitation specialists should be certain to include instruments that have been designed for and validated in populations with SCI. Finally, the results of the present study revealed that respondents with SCI reported QOL limitations mainly in diagnosis-specific domains: physical function, pain, and ability to participate. These are precisely the domains that physical rehabilitation interventions may have greatest specificity to address. Physical rehabilitation may therefore play an important role in protecting and restoring QOL after SCI.

Study limitations

The findings of this preliminary study provide a foundation for future studies with larger, more demographically representative samples. Results of the present study must be interpreted in light of the potential for bias due to the small sample size. In a validation study of the NIH Toolbox battery in respondents with neurologic disorders (Carlozzi et al., 2017), impairment rates were 13.9% and 22.2% for List Sorting and Picture Sequence, compared to 9.1% and 13.6% in the present study. Thus it appears that the present SCI cohort may have had relatively higher cognitive function than the sample included in the validation study. It should also be noted that the present cohort of individuals with SCI did not appear to have significant problems with depression or anxiety, two prevalent SHCs of SCI (Craven, Hitzig, and Mittmann, 2012). Conversely, these participants provided high self-ratings of Resilience and Positive Affect and Well-Being. Resilience, in particular, deviated strongly from the NON group and only missed achieving statistical significance because of the strict Bonferroni adjustment required by multiple statistical comparisons. Resilience has been identified as a key psychological trait that may determine adjustment, recovery, and well-being after SCI (Craig et al., 2015; Guest et al., 2015). Thus the relatively high self-rated emotional health of the present SCI cohort may not be representative of the SCI population in general. Future studies should explore possible links between cognition and QOL in people with SCI and greater psychological co-morbidity. We anticipate that robust links between cognition and QOL may exist for people with greater QOL pressures (e.g. SHCs, and social/emotional factors) or who experience cognitive impairment due to biological causes such as undiagnosed TBI, in particular.

Conclusions

Strong correlations between cognitive function, QOL, and age did not emerge in participants with SCI. Consistent with other reports, individuals living with SCI appear to recalibrate their personal expectations and assessments of QOL in ways that minimize the importance of mobility impairment. The apparent uncoupling of age and cognitive function after SCI suggests that individual injury-specific factors, many of which stem from treatable biological causes, may become key determiners of cognitive function after SCI.

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Table 1.

Subject demographics.

	Age	Gender	SCI Duration	SCI Level
SCI	19	M	4.0	C5
	24	M	4.8	C6
	47	M	30.3	C6
	51	M	19.7	C6
	25	M	4.6	C6
	34	M	2.5	C6
	30	M	5.7	C6
	27	M	0.9	C6
	49	M	19.5	C6
	48	M	2.1	C7
	59	M	11.1	C7
	37	M	15.0	T4
	53	M	16.4	T4
	37	M	14.8	T5
	62	M	22.5	T6
	68	M	20.7	T7
	37	M	10.5	T8
	38	M	16.3	T9
	73	M	10.0	T10
	26	F	0.7	T10
	35	M	10.0	T10
	69	M	22.0	T11
	47	M	7.5	T12
NON	21	F	-	-
	31	M	-	-
	58	F	-	-
	69	M	-	-
	23	F	-	-
	27	M	-	-
	24	M	-	-
	68	F	-	-
	89	M	-	-
	24	F	-	-
	24	M	-	-
	64	M	-	-
	63	M	-	-
	88	F	-	-
	23	F	-	-
	81	M	-	-

	Age	Gender	SCI Duration	SCI Level
	75	F	-	-
	23	F	-	-
	24	F	-	-
	70	M	-	-

Table 2.

Study QOL and cognition instruments.

	Metric	Domain	Sub-Domain	Score	Normative Population	Normative mean/sd
Quality of Life	EQ-5D	General QOL		QALY	U.S. general	0.866 (0.001) *
				VAS	U.S. general	80 (0.1) *
	PROMIS Global Health	General QOL	Physical Health	T-score	U.S. general	50 (10)
			Mental Health	T-score	U.S. general	50 (10)
	SCI-QOL	Physical-medical health	Pain Interference	T-score	U.S. general	50 (10)
		Emotional health	Positive Affect & Well-Being	T-score	U.S. general	50 (10)
			Anxiety	T-score	U.S. general	50 (10)
			Depression	T-score	U.S. general	50 (10)
			Resilience	T-score	SCI norming study	50 (10)
		Social participation	Ability to Participate	T-score	U.S. general	50 (10)
	SCS-M	Physical-medical	Secondary health	# SHC's	N/A	N/A
		health	conditions	Sum Score	N/A	N/A
Cognition	Dimensional Change Card Sort	Executive function	Set shifting	Unadjusted, Fully-adjusted T	U.S. general	**
	Flanker	Executive function	Attention, inhibitory control	Unadjusted, Fully-adjusted T	U.S. general	**
	List Sorting	Working memory		Unadjusted, Fully-adjusted T	U.S. general	100 (15)
	Picture Sequence	Episodic memory		Unadjusted, Fully-adjusted T	U.S. general	100 (15)

For all metrics, a higher score represents more of the concept being measured (physical health, anxiety, episodic memory, etc).

* Variation published as standard error for the EQ-5D normative population.

** Timed cognition tests: comparisons with normative data are not valid for the proctored test administration method used in this report.

Table 3.

Quality of life data.

		EQ-5D		PROMIS		SCS-M		SCI-QOL					
		QALY	**VAS**	**Physical**	**Mental**	**Sum Score**	**# SHCs**	**Pain Interference**	**PAWB**	**Anxiety**	**Depression**	**Resilience**	**Ability to Participate**
NON	Mean	0.90	84.7	46.39	49.34	3.55	2.45	45.92	60.61	48.40	44.17	46.98	54.86
	SD	0.018 *	2.43 *	4.47	4.04	5.38	3.14	6.30	5.99	8.27	6.65	11.89	7.22
SCI	Mean	0.29	80.1	38.51	47.94	13.78	8.48	52.93	58.21	50.04	47.66	56.19	46.94
	SD	0.028 *	3.68 *	4.63	4.63	7.29	3.60	8.30	6.50	7.24	7.94	7.11	6.33
	P	<0.001	0.307	<0.001	0.30	<0.001	<0.001	0.0032	0.22	0.49	0.12	0.0050	<0.001
	Effect Size	7.68		1.76		−1.90	−1.92						1.10
	Power	1.00		1.00		1.00	1.00						0.91
QUAD	Mean	0.19	77.64	35.80	47.05	13.82	8.36	51.97	57.44	51.02	48.12	54.48	43.69
	SD	0.027 *	6.83 *	2.78	5.41	6.01	2.98	8.06	5.96	7.52	9.13	6.03	4.16
PARA	Mean	0.38	82.42	41.00	48.76	13.75	8.58	53.80	58.93	49.15	47.24	57.76	49.93
	SD	0.031 *	3.49 *	4.67	3.85	8.56	4.23	8.77	7.14	7.18	7.07	7.91	6.65
	P	<0.001	0.54	0.00414	0.40	0.98	0.89	0.61	0.59	0.55	0.80	0.27	0.010
	Effect Size	1.72		1.11									
	Power	0.98		0.72									

Data shown for participants with and without SCI (top rows) and for SCI participants with quadriplegia (QUAD) vs. paraplegia (PARA)(bottom rows). Bonferroni-adjusted alpha (12 contrasts) = 0.004167. Effect size and statistical power are given for significant between-group comparisons.

* SE shown to facilitate comparisons to EQ-5D normative values, which were published as mean/SE

Table 4.

Cognition data.

		DCCS		Flanker		List Sorting		Picture Sequence	
		Unadjusted	**Fully Adjusted**	**Unadjusted**	**Fully Adjusted**	**Unadjusted**	**Fully Adjusted**	**Unadjusted**	**Fully Adjusted**
SCI	Mean	85.85	31.27	82.41	29.00	104.80	50.64	97.55	49.45
	SD	6.49	5.32	6.11	5.53	12.06	10.67	14.38	12.07
NON	Mean	87.20	33.25	85.95	32.05	105.15	52.75	113.80	62.05
	SD	9.91	7.30	7.12	7.90	17.94	7.70	23.28	13.26
	P	0.61	0.33	0.090	0.16	0.94	0.46	0.011	0.0027
	Effect Size								0.95
	Power								0.85
QUAD	Mean	85.41	28.30	81.21	27.10	105.31	47.80	96.55	47.27
	SD	6.32	4.32	7.10	4.82	16.59	15.16	14.34	10.51
PARA	Mean	86.25	33.75	83.50	30.58	104.33	53.00	98.55	51.64
	SD	6.89	4.90	5.11	5.78	6.34	4.00	15.06	13.60
	P	0.76	0.012	0.39	0.14	0.86	0.32	0.75	0.41

Data shown for participants with and without SCI (top rows) and for SCI participants with quadriplegia (QUAD) vs. paraplegia (PARA) (bottom rows). Bonferroni-adjusted alpha (8 contrasts) = 0.00625. Effect size and statistical power are given for significant between-group comparisons.

Table 5.

Pearson correlations for QOL metrics versus age and cognition. *P*-values are given for significant correlations (gray cells; $p < .05$). N/A = Fully-adjusted scale is mathematically linked to age; correlations not computed.

					EQ-5D-5L		PROMIS		SCS-M		SCI-QOL					
				Age	QALY	VAS	Physical	Mental	Sum Score	# SHCs	Pain Int.	PAWB	Anxiety	Depression	Resilience	Participation
SCI	**Age**		R^2	-	**0.209**	**0.177**	0.062	**0.244**	0.015	0.015	0.001	0.086	0.121	0.022	0.082	0.145
			P	_	**0.028**	**0.045**		**0.017**								
	DCCS	Unadjusted	R^2	0.020	0.018	0.017	0.009	0.074	0.107	0.138	0.000	0.101	0.098	0.131	0.061	0.027
			P													
		Fully-adjusted	R^2	N/A	**0.178**	**0.188**	0.107	0.113	0.008	0.001	0.005	0.035	0.046	0.002	0.059	**0.220**
			P	N/A	**0.051**	**0.039**										**0.0275**
	Flanker	Unadjusted	R^2	0.009	0.004	0.081	0.121	0.003	0.015	0.071	0.000	0.021	0.058	0.025	0.002	0.010
			P													
		Fully-adjusted	R^2	N/A	**0.223**	0.143	0.165	**0.219**	0.022	0.000	0.008	0.121	0.054	0.026	0.110	0.033
			P	N/A	**0.026**			**0.028**								
	List Sorting	Unadjusted	R^2	0.024	0.002	0.067	0.012	0.005	0.005	0.002	0.084	0.004	0.002	0.001	0.005	0.002
			P													
		Fully-adjusted	R^2	N/A	0.075	**0.206**	0.107	0.130	0.036	0.024	0.130	0.060	0.044	0.017	0.068	0.083
			P	N/A		**0.034**										
	Picture Sequence	Unadjusted	R^2	0.052	0.003	0.076	0.144	0.000	0.084	0.146	**0.226**	0.005	0.003	0.002	0.007	0.023
			P								**0.025**					
		Fully-adjusted	R^2	N/A	0.066	**0.180**	**0.274**	0.080	**0.231**	**0.305**	**0.316**	0.017	0.023	0.044	0.057	0.101
			P	N/A		**0.049**	**0.012**		**0.024**	**0.008**	**0.006**					
NON	**Age**		R^2		0.195	**0.319**	**0.413**	0.030	**0.431**	**0.454**	**0.200**	0.020	0.034	**0.291**	0.001	0.000
			P	_		**0.009**	**0.002**		**0.002**	**0.001**	**0.048**			**0.014**		
	DCCS	Unadjusted	R^2	**0.532**	**0.206**	**0.313**	**0.584**	0.000	**0.661**	**0.690**	0.093	0.087	0.079	**0.349**	0.093	0.095
			P 1	**<0.001**	**0.044**	**0.010**	**<0.001**		**<0.001**	**<0.001**				**0.006**		

				EQ-5D-5L		PROMIS		SCS-M		SCI-QOL					
			Age	QALY	VAS	Physical	Mental	Sum Score	# SHCs	Pain Int.	PAWB	Anxiety	Depression	Resilience	Participation
	Fully-adjusted	R^2	N/A	0.131	0.150	**0.208**	0.048	**0.261**	**0.221**	0.165	0.059	0.052	**0.211**	0.003	0.014
		P	N/A			**0.043**		**0.021**	**0.036**				**0.042**		
Flanker	Unadjusted	R^2	**0.563**	0.070	**0.317**	**0.387**	0.005	**0.281**	**0.407**	0.026	0.051	0.001	**0.227**	0.119	0.106
		P	**<0.001**		**0.010**	**0.003**		**0.016**	**0.002**				**0.034**		
	Fully-adjusted	R^2	N/A	0.170	**0.234**	**0.281**	0.006	**0.466**	**0.360**	**0.300**	0.041	0.005	**0.344**	0.006	0.013
		P	N/A		**0.031**	**0.016**		**<0.001**	**0.005**	**0.012**			**0.007**		
List Sorting	Unadjusted	R^2	**0.730**	0.048	**0.378**	**0.374**	0.016	**0.306**	**0.407**	0.097	0.002	0.014	**0.344**	0.035	0.030
		P	**<0.001**		**0.004**	**0.004**		**0.011**	**0.002**				**0.007**		
	Fully-adjusted	R^2	N/A	0.011	0.191	0.122	0.001	0.039	0.109	0.023	0.009	0.017	**0.200**	0.061	0.063
		P	N/A										**0.048**		
Picture Sequence	Unadjusted	R^2	**0.939**	**0.216**	**0.284**	**0.399**	0.023	**0.507**	**0.539**	0.188	0.013	0.043	0.194	0.005	0.000
		P 1	**<0.001**	**0.039**	**0.016**	**0.003**		**<0.001**	**<0.001**						
	Fully-adjusted	R^2	N/A	**0.219**	**0.299**	**0.345**	0.048	**0.448**	**0.526**	0.108	0.011	0.069	0.086	0.013	0.003
		P	N/A	**0.038**	**0.013**	**0.006**		**0.001**	**<0.001**						

Table 6.

Co-variance (Pearson R-squared) among QOL metrics.

			QALY	VAS	Physical	Mental	Sum Score	# SHCs	Pain Interference	PAWB	Anxiety	Depression	Resilience	Ability to Participate
SCI	EQ-5D	QALY	1.000											
		VAS	0.033	1.000										
	PROMIS	Phys Health T	**0.487**	0.108	1.000									
		Mental Health T	**0.228**	**0.318**	**0.198**	1.000								
	SCS-M	Sum Score	0.023	0.150	0.136	**0.283**	1.000							
		# SHC's present	0.003	0.139	0.094	**0.178**	-	1.000						
	SCI-QOL	Pain interference	0.002	0.097	0.111	0.037	**0.491**	**0.386**	1.000					
		Positive Affect	**0.197**	0.037	0.160	**0.351**	**0.399**	**0.251**	0.151	1.000				
		Anxiety	**0.292**	0.070	**0.307**	**0.314**	**0.467**	**0.358**	**0.272**	**0.545**	1.000			
		Depression	**0.213**	0.062	**0.193**	**0.399**	**0.612**	**0.436**	**0.286**	**0.629**	**0.768**	1.000		
		Resilience	**0.313**	0.044	**0.267**	**0.372**	**0.308**	**0.208**	**0.187**	**0.807**	**0.468**	**0.590**	1.000	
		Ability to Participate	**0.205**	0.151	**0.238**	**0.481**	**0.313**	**0.308**	0.069	**0.267**	**0.277**	**0.252**	**0.325**	1.000
NON	EQ-5D	QALY	1.000											
		VAS	**0.218**	1.000										
	PROMIS	Phys Health T	**0.429**	**0.500**	1.000									
		Mental Health T	0.001	0.005	0.035	1.000								
	SCS-M	Sum Score	**0.331**	0.275	**0.537**	0.025	1.000							
		# SHC's present	**0.346**	**0.404**	**0.581**	0.021	-	1.000						
	SCI-QOL	Pain interference	**0.348**	0.152	**0.211**	0.006	0.117	0.130	1.000					
		Positive Affect	0.053	0.054	0.125	0.005	0.048	0.058	0.016	1.000				
		Anxiety	0.140	0.075	0.197	0.037	0.078	0.047	0.052	**0.501**	1.000			
		Depression	0.126	0.336	**0.444**	0.009	**0.232**	**0.217**	**0.430**	0.148	0.160	1.000		
		Resilience	0.000	0.026	0.026	0.014	0.026	0.033	0.001	**0.412**	0.141	**0.228**	1.000	
		Ability to Participate	0.076	0.040	0.160	0.000	0.009	0.045	0.144	**0.468**	**0.224**	**0.323**	**0.270**	1.000

Significant correlations ($p < .05$) are denoted as gray cells. Sum Score and #SHCs are mathematically related; correlations not computed.